REMARKS

Claims 160-177 and 237-272 are pending. Claims 240 and 272 are amended to correct typographical errors. Claim 160 has been amended to recite that the features are present in a pattern on the surface.

As an initial matter, Applicants respectfully note that although claim 272 is listed as rejected in the Disposition of the Claims, it is not included in any of the rejections set forth on pp. 2-7. Clarification is respectfully requested.

Applicants note that the Examiner has withdrawn the rejections that used Palsson's U.S. Pat. No. 5,811,274 in favor of rejections that use corresponding PCT publication WO 96/17948.

Rejections under 35 U.S.C. 102

Claims 160-163, 166, 169, 172, 175, 241, 242, 242-248, 251, 253, 254, 257, 259, 260, 263, 265, 266, 269 and 271 are rejected as allegedly anticipated by WO 96/17948, hereinafter "Palsson." The Examiner asserts that Palsson teaches "a support comprising nucleic acids deposited at a plurality of distinct locations (i.e., discrete) and plating dispersed eukaryotic cells on top of the nucleic acids (i.e., the plurality of locations comprise eukaryotic cells and nucleic acids in discrete locations)." Applicants respectfully traverse the rejection and request reconsideration.

Applicants' previous response (filed October 2, 2009) pointed out that Palsson's US Patent No. 5,811,274, which corresponds to WO 96/17948, does not teach a surface having a plurality of locations, wherein each location comprises eukaryotic cells and a feature comprising one or more defined nucleic acid molecules in a discrete location. Applicants respectfully submit that the Examiner has not addressed Applicants' arguments, which apply equally to WO 96/17948 as they do to U.S. Pat. No. 5,811,274. Applicants respectfully submit that the portions of Palsson cited by the Examiner do not describe a surface having a plurality of locations, each comprising "a feature comprising one or more defined nucleic acids in a discrete location." For example, p. 5, line 29 – p. 6, line 10, of WO 96/17948 state as follows: "This invention provides a method of transfecting target cells by particles comprising depositing the particles on a cell growth support and contacting the target cells with the particle-loaded cell growth support. In

one embodiment of the method, the particles are retroviral particles. Another embodiment further comprises cryopreserving or lyophilizing the particle-loaded cell growth support prior to contacting target cells. The invention also provides a composition comprising particles capable of transfecting target cells localized on a filter, membrane filter, cell culture surface or tissue engineering material in an amount effective for increasing the transfection efficiency of target cells ....." Page 8, lines 1-15, of WO 96/17948 state as follows: "The invention provides a new method that dramatically increases the transfection efficiency by increasing the contact between particles and target cells. The contact is increased by localizing particles on a cell growth support and directing target cells to contact the particle-loaded cell growth support. As broadly claimed, the method comprises two steps. First, the particles are deposited on the cell growth support by various means such as filtration or absorption. Second, the target cells are directed to the particle-loaded cell growth support by various means such as gravity sedimentation or filtration. Localizing the particles on the cell growth support increases the contact between particles and target cells, which increases the transfection efficiency compared with that ....." Applicants respectfully submit that there is no teaching in the portions of Palsson reproduced above (or in the other portions of Palsson cited by the Examiner) describing nucleic acids present on the support in a plurality of discrete locations so as to result in features, each comprising an area of a substrate having a defined nucleic acid sequence affixed thereto (or sequences in the case of certain co-transfection embodiments). Applicants respectfully submit that one of skill in the art would understand that the term "discrete location" as used in the instant claims indicates that the nucleic acids are confined to particular areas of the surface rather than being distributed throughout the surface. Thus, the surface must contain regions between the features, which regions do not contain the defined nucleic acids that are present in the features. Applicants respectfully submit that Palsson does not teach confining defined nucleic acids to particular locations on the surface and thus does not teach a surface comprising a plurality of features as set forth in the instant claims. For at least this reason, Applicants respectfully submit that Palsson does not teach all the features of the claims and thus cannot anticipate the claims. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. 103(a)

Claims 160-166, 169, 172, 173, 175, 241-248, 251, 253, 254, 257, 259, 260, 263, 265, 266, 269, and 271 are rejected as allegedly unpatentable over Palsson. As discussed above, Applicants respectfully submit that Palsson does not teach a surface comprising a plurality of features as set forth in the instant claims. For at least this reason, Applicants respectfully submit that the rejection should be withdrawn.

Claims 160-164, 166-177, 237-242, and 244-271 are rejected as allegedly unpatentable over Palsson, in view of both Taylor et al. (U.S. Pat. No. 6,103,479) and Fire (U.S. Pat. No. 6,506,559). The Examiner acknowledges that Palsson does not teach a microarrayer, wherein use of the microarrayer results in rows and columns comprising different nucleic acids at different locations but contends that doing so is suggested by Taylor. The Examiner also contends that Taylor teaches high throughput screening (HTS) of nucleic [acids] (*sic*) by using arrays comprising tens of thousands of nucleic acid discrete spots, wherein the arrays are made by using a microarrayer, and where the location of the spot provides the address for later reference to each nucleic acid spot. The Examiner also contends that Taylor teaches HTS of responses of cells to biologically active compounds. Based on these alleged teachings, the Examiner contends it would have been obvious to modify Palsson according to the teachings of Taylor to obtain the "predictable result of obtaining a transfection surface suitable for HTS of cellular response to diverse biologically active factors encoded by nucleic acids." Applicants respectfully traverse the rejection and request reconsideration.

Column 1, lines 47-56 of Taylor, cited by the Examiner, describes arrays composed of 10-14 nucleotide oligonucleotides attached to a glass plate, available commercially from Affymetrix under the trade name GENECHIP™. The oligonucleotides are intended to hybridize to fluorescently labeled complementary nucleic acids, which can then be detected after washing to remove nucleic acids that did not hybridize to oligonucleotides on the array (Taylor, col. 1, lines 56-60). The Examiner asserts that, "the arrays are made by using a microarrayer." Applicants respectfully submit that Taylor is silent as to how the oligonucleotide arrays were made. The Examiner has not provided any evidence that the arrays were made by using a

microarrayer. Accordingly, to the extent that the rejection is based on the premise that the oligonucleotide arrays described by Taylor were made using a microarrayer, Applicants respectfully submit that it is unsupported and respectfully request that it be withdrawn.

Furthermore, Applicants respectfully submit that, for at least each of the following reasons, the Examiner has failed to establish that one of skill in the art would be motivated to modify Palsson according to the teachings of Taylor to arrive at the instant invention with a reasonable expectation of success.

First, Applicants submit that Taylor does not suggest or provide motivation for combining oligonucleotide arrays with cell arrays for HTS screening. Taylor does not teach or suggest that oligonucleotide arrays could have any use other than for detecting fluorescently labeled complementary nucleic acids. Taylor does not teach or suggest that such arrays could have any use whatsoever in the context of cultured cells.

Second, there is nothing in Taylor to suggest that the conditions under which oligonucleotide arrays are made result in a surface compatible with the growth and transfection of eukaryotic cells. Applicants respectfully submit that the Examiner has failed to establish that such an oligonucleotide array could predictably be used to produce an array of transfected eukaryotic cells growing in culture on the surface of such oligonucleotide array.

Third, Applicants submit that in order for the GENECHIP array to be useful for the purpose described by Taylor, i.e., hybridization of oligonucleotides to fluorescently labeled complementary nucleic acids, one of skill in the art would find it desirable that the oligonucleotides remain attached to the glass plate during the processes of hybridization, washing to remove unhybridized nucleic acids, and detection. Applicants respectfully submit that the principle of operation of an oligonucleotide array such as that mentioned by Taylor is based on oligonucleotides that remain attached to the surface. If oligonucleotides detach from the surface they would not contribute to the detection of labeled complementary nucleic acids and, if anything, would reduce their detection. However, the instant invention requires that nucleic acids are introduced into and transfect eukaryotic cells. Nucleic acids that remain attached to a surface would not be capable of entering and transfecting cells. Applicants respectfully direct the Examiner's attention to MPEP 2143.01 VI, entitled "The Proposed Modification Cannot Change the Principle of Operation of a Reference." As stated therein, "If

the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (CCPA 1959)." Applicants acknowledge that as set forth in the rejection, the "prior art invention being modified" is Palsson rather than Taylor. However, Applicants respectfully submit that the reasoning of MPEP 2143.01 VI is applicable - the modification proposed by the Examiner would change the principle of operation of the oligonucleotide array of Taylor from one that is based on oligonucleotides that remain attached to the surface to one in which at least some detachment from the surface is required. Applicants submit that one of skill in the art would not be motivated to make the modification proposed by the Examiner.

Fourth, even if the skilled artisan was motivated to modify Palsson by using the oligonucleotide array of Taylor, which Applicants submit would not be the case, there is no evidence in Taylor that oligonucleotides of the GENECHIP array would in fact detach from the surface and enter eukaryotic cells, let alone that they would do so in a manner that would predictably result in an array of transfected eukaryotic cells. Applicants respectfully submit that the Examiner has failed to establish that an oligonucleotide array such as that mentioned by Taylor could predictably be used to produce an array of transfected eukaryotic cells growing in culture on the surface.

In summary, Applicants respectfully submit that there is no motivation to combine Taylor and Palsson as the Examiner suggests. Even if the skilled artisan were motivated to attempt to combine Taylor and Palsson as suggested by the Examiner, there would be no reasonable expectation, based on the cited art, of success in arriving at the claimed invention.

With regard to claims 170, 171, 176, 177, 249, 250, 252, 255, 256, 258, 261, 262, 264, 267, 268, and 270, the Examiner acknowledges that Palsson and Taylor do not teach siRNA but contends, citing Fire, that "doing so is suggested by the prior art.." Claims 170, 171, 176, 177, 249, 250, and 252 depend on claims 160. Claim 255, 256, and 258 depends on claim 253. Claims 261, 262, and 264 depends on claim 259. Claims 267, 268, and 270 depend on claim 256. Applicants respectfully submit that the combination of Palsson and Taylor does not teach or suggest the invention of any of independent claims 160, 237, 238, 253, or 259. Fire adds nothing in this regard. For at least this reason, Applicants submit that the combination of Palsson,

Taylor, and Fire (even if the combination of Palsson and Taylor as suggested by the Examiner were permissible, which Applicants submit is not the case) does not render any of claims 170, 171, 176, 177, 249, 250, 252, 255, 256, 258, 261, 262, 264, 267, 268, or 270 obvious.

In summary, Applicants were the first to recognize the feasibility and desirability of reverse transfecting populations of cells in parallel with distinct, defined nucleic acids affixed to a surface at discrete locations. Applicants also recognized that microarrayers could be used to affix nucleic acids to surfaces for purposes of reverse transfection. Applicants respectfully submit that none of Palsson, Taylor, or Fire, either alone or in combination, renders any of the claims obvious, and respectfully request that the rejection be withdrawn.

CONCLUSION

In conclusion, Applicant submits that the claims are in condition for allowance, and such action is respectfully requested. Enclosed is a Petition to extend the period for replying to the Office action for three months, to and including June 30, 2010, and payment of the required extension fee. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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